September 20, 2007

Matt Whitworth
First Assistant United States Attorney
Charles Evans Whitaker Courthouse
400 East 9th St; 5th floor
Kansas City, MO 64106

*REPORT ADDENDUM*
Re: US v Lisa M. Montgomery
No. 05-06002-01-CR-SJ-GAF

Dear Mr. Whitworth,

We have now had the opportunity to examine the data that was used to generate Fig 4. We have each independently evaluated the provided new data and have come to the identical conclusions. Those conclusions are summarized below.

As stated in our initial reports and at the time of our respective hearing testimonies, there was concern that the method to generate the Region/Whole Brain ratios (normalization) was likely different for the Controls than for the defendant, and as such, was a potential source of methodological error. We further emphasized that such an error would result in invalid conclusions regarding whether Lisa Montgomery's PET scan could be considered abnormal based on generally accepted scientific standards.

Dr. Gur testified both at the hearing and in written correspondence with us prior to the hearing that he had calculated a true Whole brain value for both Lisa Montgomery (LM) and the controls (CON) and did NOT merely take the average of the 36 grey matter regions (GM ROIs) for either group (LM or CON). Verification that the control data was indeed calculated as described is critical, as it is the sole foundation for the opinion that LM has multiple regions of abnormal metabolism. Furthermore, such regional abnormalities were the primary basis for further conclusions about LM's behavior and disease risk.

Dr. Gur provided us with what he stated was the raw data used to generate the Region/WB ratios contained in Figure 4 (copied below). We have re-calculated the Region/WB ratios from this raw data and plotted the data in a manner similar to that found in Figure 4 to verify that the figure truly does reflect his stated method of analysis.

We received the following raw data from the 23 controls:

(1) Raw activity values for 35 ROIs, sampled using an ROI template provided by Dr. Gur.
(2) The true Whole Brain activity value for each control subject.

**A. Missing data.**

Data for a single ROI appears to be missing for each of the 23 control subjects. There are 36 ROIs in Figure 4 and only 35 ROIs in the raw data provided by Dr. Gur. Following the Region/WB ratio calculation below, and comparisons of the CON graphs to Figure 4, it appears that the 4th region from the right is missing which is the Hypothalamus. This region was provided for LM. We performed the analyses on the data provided, e.g. 35 Regions.

N.B. The omission of one ROI has no effect on the key issue of normalization. We accounted for its absence in reproducing Fig 4a of Dr. Gur's report. We note this for completeness.

**B. Method 1: Calculation of Region/WB ratios using True WB values.**

For the 35 regional values available for LM and the 23 controls, the R/WB ratios were calculated and the mean for the 23 subjects plotted with 1 Standard Deviation (Figure 1 below) to reproduce Dr. Gur's Green line in Figure 4 of his report (copied below, under Figure 1). Our newly generated Region/WB plot (fig 1) does match his Figure 4, suggesting that the Region/WB ratios in his report were not calculated as stated. In Figure 1 below: the maximum mean R/WB value is 1.4 with only 5 regions having a mean value less than 1.0. This is in distinction to the control graph in Figure 4, where the max value for any of the 36 regions is 1.2, with 13 regions having a R/WB ratio less than 1.0.

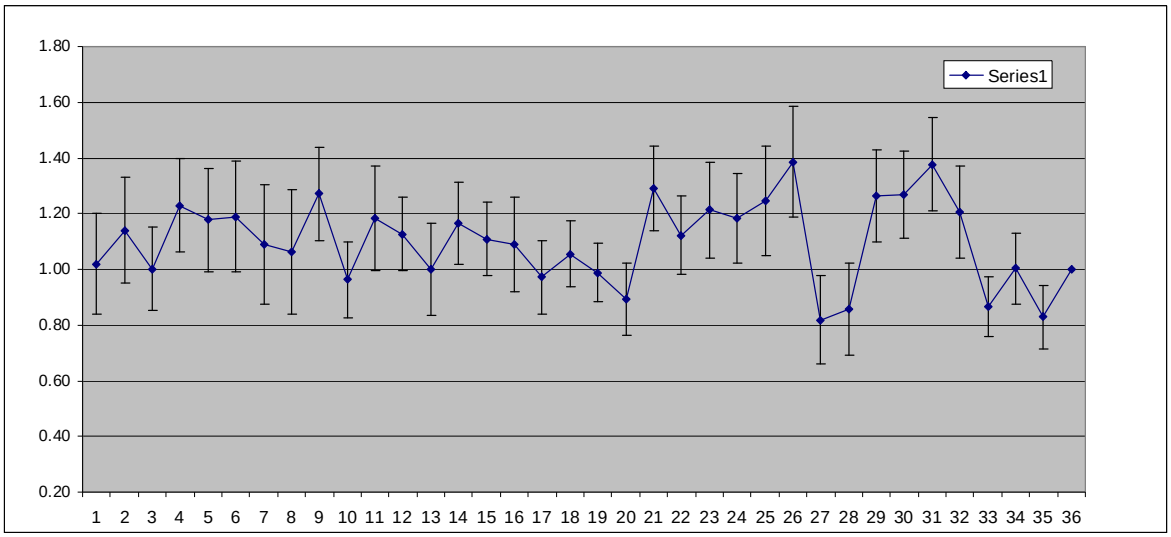



Figure 1. R/WB ratio generated using True WB values provided (new data)

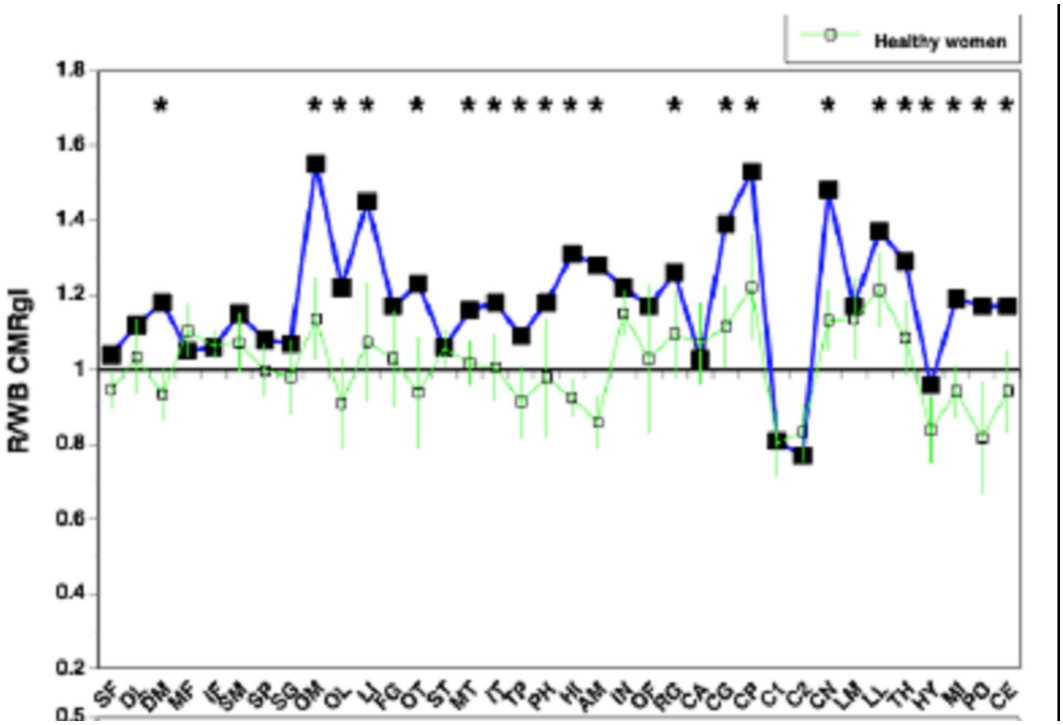



Figure 4 from Dr. Gur's Expert Report, 8/23/07

**C. Method 2: Calculation of Region/WB ratio using the average of the 35 ROIs (GM).** As postulated in our testimony and reports, the likely source of this discrepancy is use of a different WB value for calculating the Region/WB ratios. To confirm this, we recalculated the Region/WB ratios using the average of the 35 regions for the denominator (GM). The graph generated from this calculation produced a graph that matches the control values in Dr. Gur's report, Figure 4. (FIGURE 2)

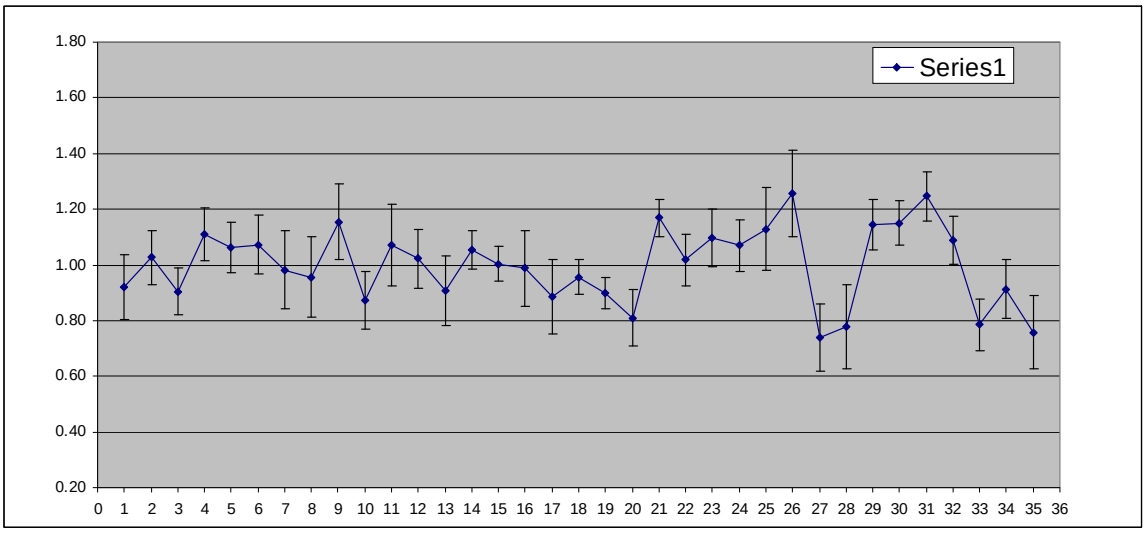



Figure 2. R/WB ratio generated using average of 35 ROIS (GM) for the WB value

**D. Comparison of the two methods.** As seen in Figure 3 below, there is a systematic difference in the control curves for the Region/WB values, depending the method used to generate the WB. Region/WB values calculated using the True WB (upper line) are higher than the ratio calculated using the 35 region average (lower line). The lower line appears to match the Control graph in Dr. Gur's Report, Fig 4. We conclude that the method used by Dr. Gur to calculate the Control Ratios used a different method than used for the defendant, making the comparison invalid.

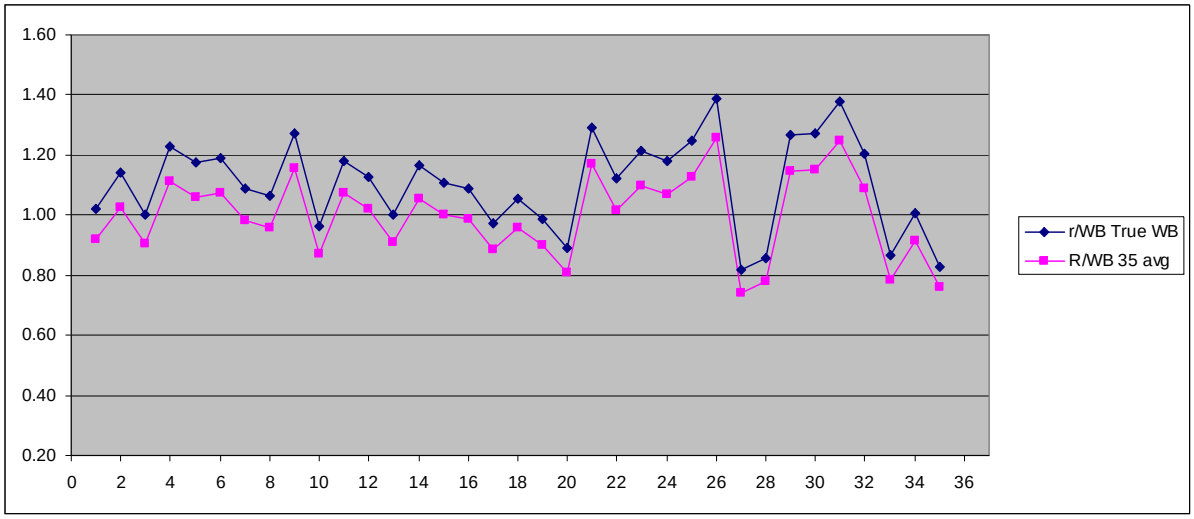
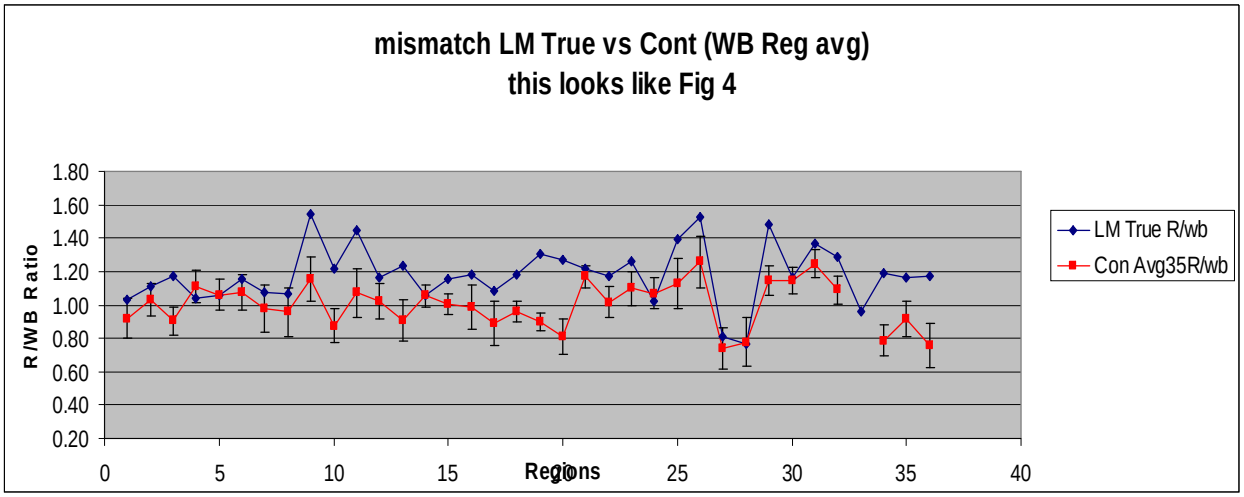
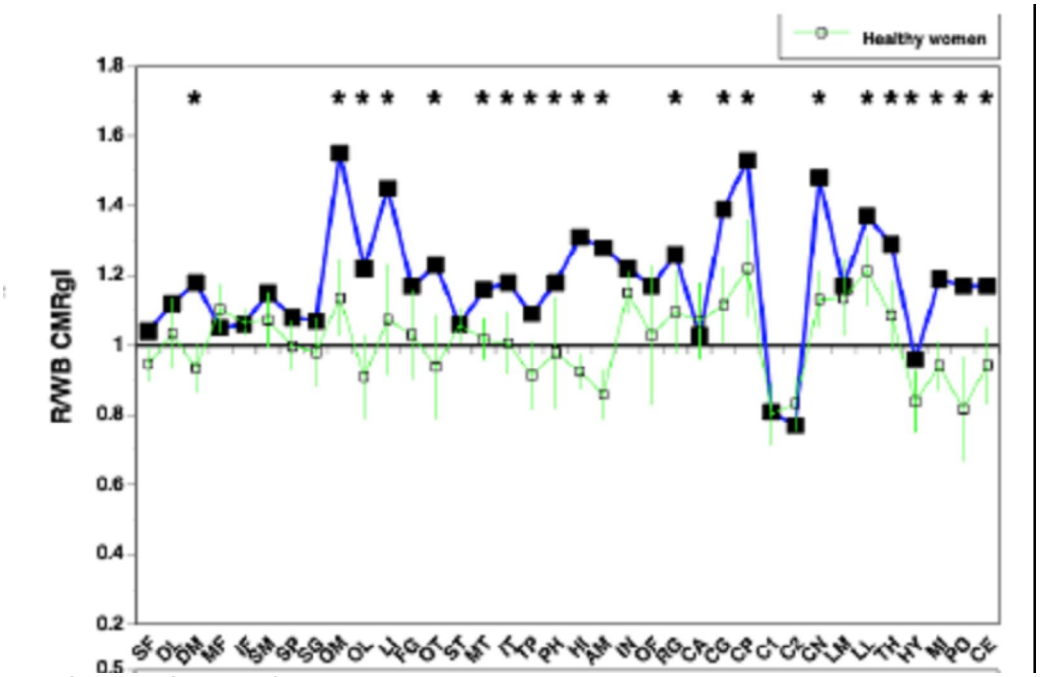



Figure 3. R/WB ratio generated using True WB (top line) versus the 35 Reg Avg (lower line)

**E. Consequences of using different normalization methods for LM and Controls.**
As discussed at the hearing and in our written reports, it is not methodologically valid to compare scans that have used two different methods of normalization. Examination of the raw data provided by Dr. Gur and recalculation of the Region/WB ratios using the 2 possible methods proves that LM was normalized using the True WB value whereas the Controls were normalized using the 35 region Average (GM). This is an invalid comparison, and therefore is not reliable to conclude that LM has abnormal brain metabolism since her scan was not compared to the controls using a comparable normalization method. Failure to match the normalization method has introduced a predictable error resulting in apparent differences between LM and the Control group that do not exist. To illustrate this point, we have graphed LM normalized to the true WB vs the Controls normalized the the 35 ROI average. This graph (#1) is identical to that contained in Figure 4 in Dr. Gur's report.

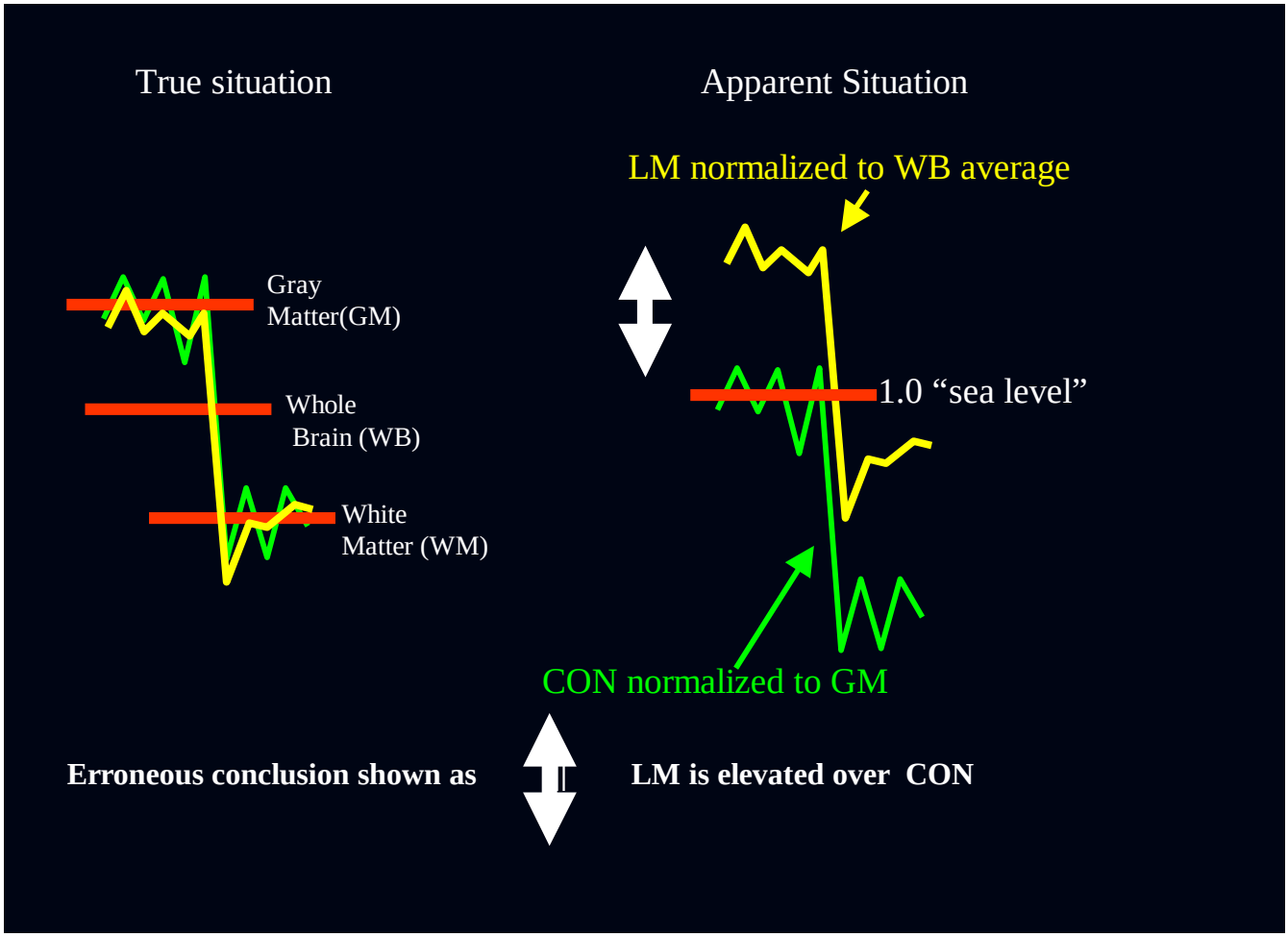
Graph #1: LM calculated with True WB v Controls calculated using 35ROI average.



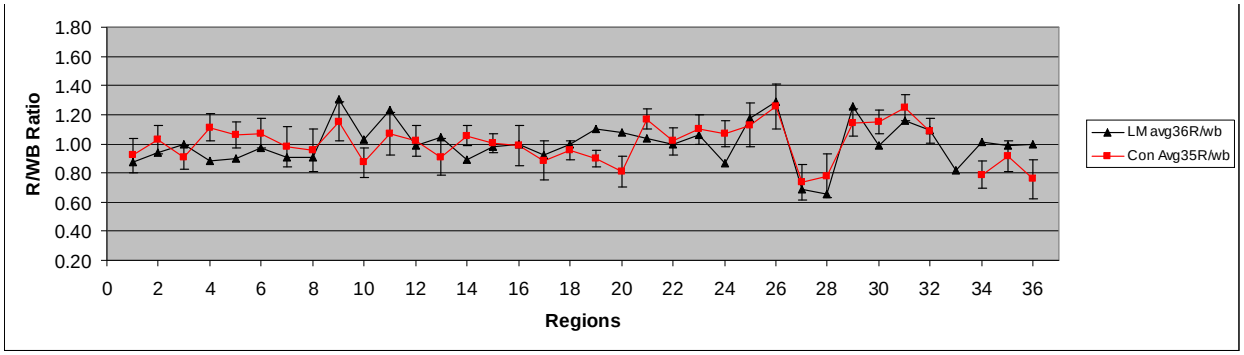

Graph #2: Figure 4 from Dr. Gur's Report

**F. Schematic of error made in normalization, illustrating apparent difference between defendant (LM) and healthy control (CON) population.**

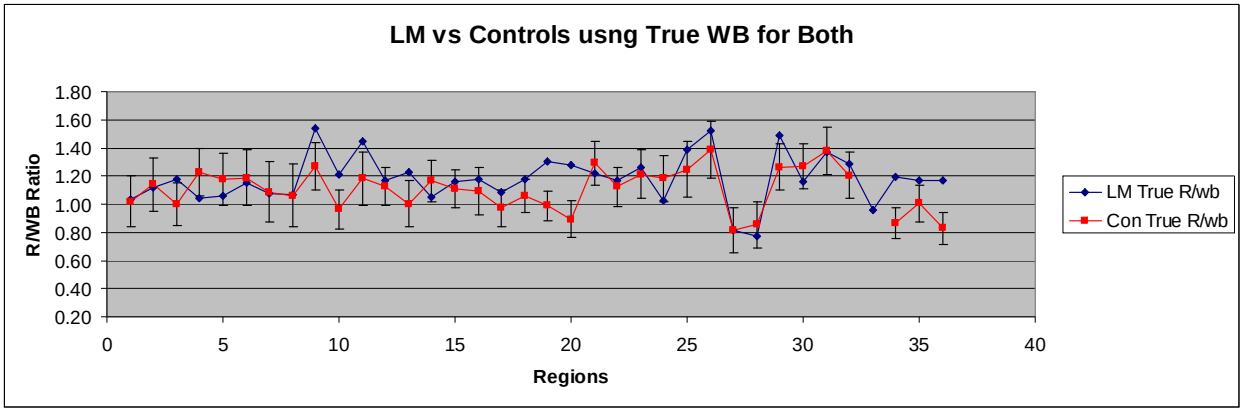



"Normalization" is like defining "sea-level" for estimating the height of a mountain.The figure shows that if one measures the yellow curve (LM) relative to an average gray matter (GM) reference point (sea-level) but measures the green curve relative to the lower whole-brain (WB) reference point, then the LM values will erroneously appear to be higher. It is essential that the same reference point be used for both LM and the CON group.

**G. Re-calculation of LM vs Controls using the same normalization method.** The many regions reported as abnormal in LM are no longer significantly different from the Controls when an appropriate analysis is performed using comparable normalization methods. Graph 3 shows a comparison using the average of all 35 regions. Graph 4 shows a comparison using the True WB mean values.




Graph #3: LM normalized to the 35 ROI average (GM) vs the Controls using the same method, Error bars are 1 standard deviation (SD). No areas of significant difference (> or < 2SD)




Graph #4: LM normalized to the true WB vs the Controls using the same method, Error bars again show 1 Standard Deviation.

Note larger standard deviation in controls with True WB method
One region just exceeds 2SD, the amygdala. The laterality values confirm the left is normal, the right is higher than controls. The other 20 regions previously reported as abnormal are now not significantly different from the controls.

**Conclusions:**

1. Figure 4 in Dr. Gur's report is not an accurate representation of the methods he claimed he used for the analysis (True WB value for both Controls and LM).
2. The comparison of data in Controls normalized using one method to the defendant normalized using a different method was the basis to conclude that LM's brain metabolism in 21 regions was abnormal.
3. Such a comparison is methodologically invalid and any conclusions drawn from such a contrast are therefore also invalid.
4. An appropriate comparison using the same normalization strategy (either True WB or the average of the 35 regions) failed to reproduce Dr. Gur's abnormal findings in Figure 4.
5. The data demonstrate no significant differences (greater than 2SD) between the Control group and the defendant.
6. No behavioral or diagnostic conclusions can be made from these data.
7. As previously stated, there is no scientific or medical precedent to use FDG PET to diagnose any psychiatric diagnosis. More specifically, there is no precedent to either diagnose pseudocyesis or a vulnerability to pseudocyesis, since this disorder has never been studied using FDG and as such, there is no reliable PET pattern for this disorder. The point is now moot, as an appropriate reanalysis of Dr. Gur's primary data demonstrates that none of the findings previously reported are present.

Sincerely,

Helen Mayberg MD
Alan Evans, PhD